

SUPPLEMENTARY MATERIAL

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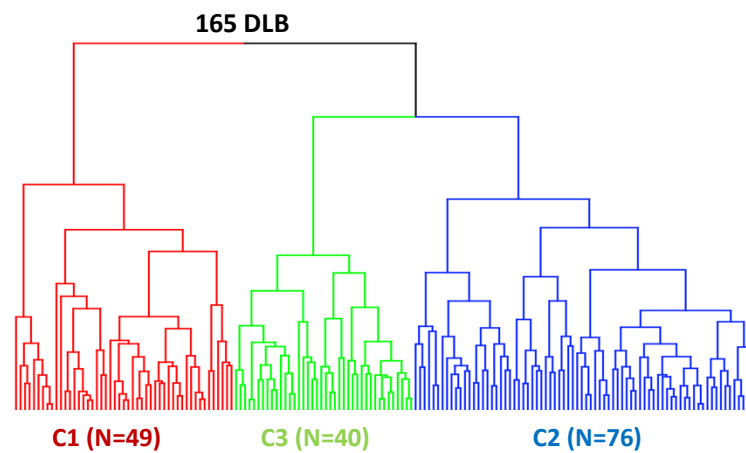
Supplementary Table 1. List of ROIs used in the cluster analysis.

LIST OF ROIs ENTERED IN THE ANALYSIS
Precentral bilateral
Frontal Sup bilateral
Frontal Sup Orb bilateral
Frontal Mid bilateral
Frontal Mid Orb bilateral
Frontal Inf Oper bilateral
Frontal Inf Tri bilateral
Frontal Inf Orb bilateral
Rolandic Oper bilateral
Supp Motor Area bilateral
Olfactory bilateral
Frontal Sup Medial bilateral
Frontal Med Orb bilateral
Rectus bilateral
Insula bilateral
Cingulum Ant bilateral
Cingulum Mid bilateral
Hippocampus bilateral
Amygdala bilateral
Calcarine bilateral
Cuneus bilateral
Lingual bilateral
Occipital Sup bilateral
Occipital Mid bilateral
Occipital Inf bilateral
Fusiform bilateral
Postcentral bilateral
Parietal Sup bilateral
Parietal Inf bilateral
SupraMarginal bilateral
Angular bilateral
Precuneus bilateral
Paracentral lobule bilateral
Caudate bilateral
Pallidum bilateral
Putamen bilateral
Thalamus bilateral
Heschl bilateral
Temporal Sup bilateral
Temporal Pole Sup bilateral
Temporal Mid bilateral
Temporal Pole Mid bilateral
Temporal Inf bilateral
Pons
Dorsal Mesopontine
Entorhinal Cortex bilateral
ParaHippocampal bilateral
Cingulum Post bilateral
Retrosplenial Cortex bilateral

Appendix 1. Longitudinal analysis of MMSE trajectories.

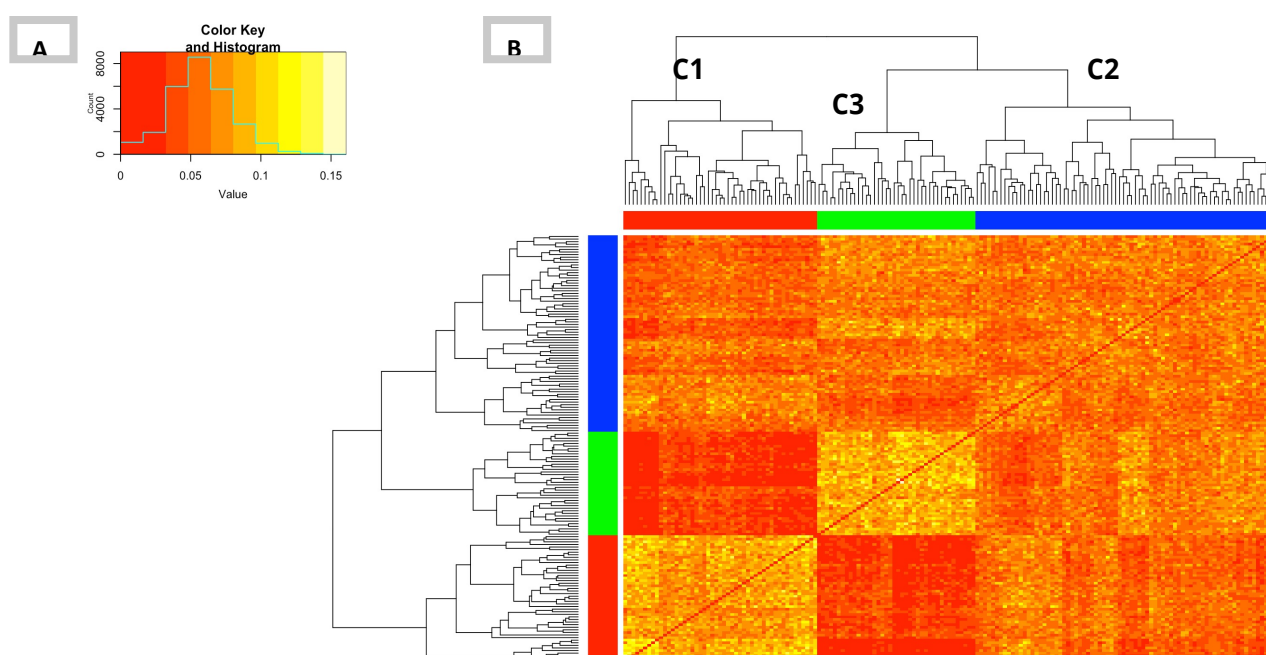
The linear mixed effects model (LMM) was conducted in R version 4.0.3 using the lme4 package. The design consisted of a random intercept per subject with the model reference set to the baseline and cluster 3. The outcome was the longitudinal MMSE scores (12-month, 24-month and 36-month follow-up). The fixed effects were time (categorical), cluster (categorical) and interaction between time and cluster. Post-hoc pairwise comparisons were done between clusters based on model estimates with multiple comparisons corrections with Tukey adjustment (using emmeans package).

Supplementary Figure 1. Dendrogram from the cluster analysis.



Dendrogram of the 165 patients with pDLB clustered according to gray matter volumes.
Abbreviations: C1 – Cluster 1, C2 – Cluster 2, C3 – Cluster 3, DLB – Dementia with Lewy bodies.

Supplementary Figure 2. Random forest proximity matrix assessment.



(A) Histogram with the color key: values closer to 0 indicate non-similar observations while values closer to 1 indicate identical observations. Pairwise similarities shown in red are the most stable, while similarities shown in yellow are the least stable. Hence, findings are stable when values are closer to 0. (B) Matrix showing the average difference between the similarity matrix used as the input of the cluster analysis (the main analysis) and the similarity matrices obtained from the simulated 100 random forest models. The clustering dendrogram is displayed in the horizontal and vertical axes. Abbreviations: C1 – Cluster 1 (cortical predominant subtype); C2 - Cluster 2 (fronto-occipital predominant subtype); C3 – Cluster 3 (subcortical predominant subtype).

Supplementary Table 2. Regional differences between clusters.

	C1 (n=49)	C2 (n=76)	C3 (n=40)	C1 z-scores	C2 z-scores	F ANCOVA	FDR adjusted p-values	post-hoc paired test
Precentral_L	-0.717 (1.058)	0.081 (1.156)	0.723 (0.972)	-1.4814	-0.6598	24.943	1.37E-09	C1 < C2, C1 < C3, C2 < C3
Precentral_R	-0.613 (1.366)	0.038 (1.032)	0.679 (1.134)	-1.1395	-0.5652	17.002	3.56E-07	C1 < C2, C1 < C3, C2 < C3
Frontal_Sup_L	-0.471 (0.944)	0.028 (0.983)	0.522 (1.024)	-0.9707	-0.4821	14.044	3.42E-06	C1 < C2, C1 < C3, C2 < C3
Frontal_Sup_R	-0.365 (0.995)	-0.138 (1.033)	0.709 (0.875)	-1.2271	-0.968	17.731	2.11E-07	C1 < C3, C2 < C3
Frontal_Sup_Orb_L	-0.259 (0.307)	0.017 (0.298)	0.283 (0.262)	-2.0651	-1.0107	50.636	1.19E-16	C1 < C2, C1 < C3, C2 < C3
Frontal_Sup_Orb_R	-0.277 (0.328)	0.027 (0.310)	0.288 (0.384)	-1.4728	-0.6797	41.743	1.98E-14	C1 < C2, C1 < C3, C2 < C3
Frontal_Mid_L	-0.666 (1.946)	-0.053 (1.940)	0.917 (2.352)	-0.6733	-0.4125	8.104	0.0005126 32	C1 < C3, C2 < C3
Frontal_Mid_R	-0.858 (1.914)	0.076 (1.913)	0.906 (1.961)	-0.9001	-0.423	11.519	2.70E-05	C1 < C2, C1 < C3, C2 < C3
Frontal_Mid_Orb_L	-0.381 (0.440)	0.028 (0.463)	0.412 (0.494)	-1.6066	-0.7763	42.525	1.42E-14	C1 < C2, C1 < C3, C2 < C3
Frontal_Mid_Orb_R	-0.382 (0.486)	0.104 (0.453)	0.270 (0.422)	-1.547	-0.3942	32.574	7.04E-12	C1 < C2, C1 < C3, C2 < C3
Frontal_Inf_Oper_L	-0.169 (0.562)	-0.056 (0.529)	0.313 (0.629)	-0.7668	-0.5877	10.622	5.79E-05	C1 < C3, C2 < C3
Frontal_Inf_Oper_R	-0.369 (0.432)	0.034 (0.457)	0.387 (0.635)	-1.192	-0.5554	32.956	5.65E-12	C1 < C2, C1 < C3, C2 < C3
Frontal_Inf_Tri_L	-0.337 (0.576)	0.062 (0.537)	0.293 (0.575)	-1.0969	-0.4013	18.469	1.23E-07	C1 < C2, C1 < C3, C2 < C3
Frontal_Inf_Tri_R	-0.328 (0.569)	0.003 (0.615)	0.395 (0.564)	-1.2838	-0.6958	20.859	2.22E-08	C1 < C2, C1 < C3, C2 < C3
Frontal_Inf_Orb_L	-0.525 (0.664)	0.152 (0.527)	0.352 (0.510)	-1.7178	-0.3905	39.274	9.45E-14	C1 < C2, C1 < C3, C2 < C3
Frontal_Inf_Orb_R	-0.462 (0.634)	0.094 (0.522)	0.387 (0.579)	-1.468	-0.5052	33.306	4.71E-12	C1 < C2, C1 < C3, C2 < C3
Rolandic_Oper_L	-0.282 (0.354)	-0.014 (0.348)	0.374 (0.418)	-1.5702	-0.9309	46.489	1.23E-15	C1 < C2, C1 < C3, C2 < C3
Rolandic_Oper_R	-0.352 (0.487)	0.011 (0.422)	0.409 (0.518)	-1.4695	-0.768	38.287	1.59E-13	C1 < C2, C1 < C3, C2 < C3
Supp_Motor_Area_L	-0.502 (0.563)	0.110 (0.710)	0.406 (0.894)	-1.0154	-0.3307	23.672	3.01E-09	C1 < C2, C1 < C3, C2 < C3
Supp_Motor_Area_R	-0.409 (0.627)	0.026 (0.886)	0.452 (0.902)	-0.9555	-0.4725	15.102	1.49E-06	C1 < C2, C1 < C3, C2 < C3
Olfactory_L	-0.037 (0.096)	0.001 (0.089)	0.0438 (0.105)	-0.7712	-0.4028	9.873	0.0001097 14	C1 < C2, C1 < C3, C2 < C3
Olfactory_R	-0.043 (0.104)	0.001 (0.101)	0.051 (0.108)	-0.873	-0.4717	11.3	3.23E-05	C1 < C2, C1 < C3, C2 < C3
Frontal_Sup_Medial_L	-0.345 (0.830)	-0.105 (0.839)	0.623 (0.923)	-1.0496	-0.7893	18.695	1.07E-07	C1 < C3, C2 < C3

	C1 (n=49)	C2 (n=76)	C3 (n=40)	C1 z-scores	C2 z-scores	F ANCOVA	FDR adjusted p-values	post-hoc paired test
Frontal_Sup_Medial_R	-0.297 (0.962)	-0.051 (1.130)	0.462 (1.064)	-0.7147	-0.4832	6.999	0.0013428 15	C1 < C3, C2 < C3
Frontal_Med_Orb_L	-0.332 (0.372)	0.055 (0.379)	0.302 (0.300)	-2.1163	-0.8252	47.162	9.07E-16	C1 < C2, C1 < C3, C2 < C3
Frontal_Med_Orb_R	-0.273 (0.445)	0.083 (0.438)	0.176 (0.297)	-1.5128	-0.3136	19.379	6.43E-08	C1 < C2, C1 < C3
Rectus_L	-0.1553 (0.285)	0.037 (0.238)	0.118 (0.324)	-0.8434	-0.2477	14.799	1.86E-06	C1 < C2, C1 < C3
Rectus_R	-0.154 (0.241)	0.053 (0.251)	0.087 (0.265)	-0.9096	-0.1251	15.736	9.16E-07	C1 < C2, C1 < C3
Insula_L	-0.454 (0.408)	0.043 (0.439)	0.473 (0.482)	-1.9224	-0.8898	67.639	1.14E-20	C1 < C2, C1 < C3, C2 < C3
Insula_R	-0.534 (0.477)	0.109 (0.419)	0.447 (0.536)	-1.8311	-0.6311	71.318	6.34E-21	C1 < C2, C1 < C3, C2 < C3
Cingulum_Ant_L	-0.163 (0.508)	-0.052 (0.555)	0.300 (0.578)	-0.8026	-0.6107	10.378	7.09E-05	C1 < C3, C2 < C3
Cingulum_Ant_R	-0.241 (0.650)	-0.094 (0.806)	0.476 (0.662)	-1.0838	-0.8614	14.444	2.47E-06	C1 < C3, C2 < C3
Cingulum_Mid_L	-0.109 (0.384)	-0.039 (0.304)	0.209 (0.408)	-0.7801	-0.6098	11.748	2.24E-05	C1 < C3, C2 < C3
Cingulum_Mid_R	-0.219 (0.368)	0.026 (0.398)	0.217 (0.403)	-1.0806	-0.4711	17.428	2.60E-07	C1 < C2, C1 < C3, C2 < C3
Hippocampus_L	-0.145 (0.354)	-0.010 (0.342)	0.199 (0.281)	-1.2253	-0.746	14.798	1.86E-06	C1 < C2, C1 < C3, C2 < C3
Hippocampus_R	-0.152 (0.390)	0.011 (0.298)	0.165 (0.256)	-1.2364	-0.6001	13.513	5.23E-06	C1 < C2, C1 < C3, C2 < C3
Amygdala_L	-0.034 (0.093)	0.001 (0.110)	0.040 (0.079)	-0.9404	-0.4915	7.723	0.0011162 79	C1 < C3
Amygdala_R	-0.059 (0.104)	0.010 (0.101)	0.051 (0.086)	-1.288	-0.4762	18.038	1.71E-07	C1 < C2, C1 < C3, C2 < C3
Calcarine_L	-0.183 (0.814)	-0.188 (0.760)	0.582 (0.843)	-0.9075	-0.9136	16.618	4.80E-07	C1 < C3, C2 < C3
Calcarine_R	-0.290 (0.757)	-0.082 (0.724)	0.512 (0.895)	-0.8958	-0.6639	15.334	1.26E-06	C1 < C3, C2 < C3
Cuneus_L	-0.370 (0.7851)	-0.094 (0.742)	0.634 (0.917)	-1.0948	-0.7944	22.928	4.95E-09	C1 < C2, C1 < C3, C2 < C3
Cuneus_R	-0.405 (0.708)	0.001 (0.718)	0.494 (0.848)	-1.0608	-0.5811	19.939	4.39E-08	C1 < C2, C1 < C3, C2 < C3
Lingual_L	-0.547 (0.867)	0.008 (0.995)	0.655 (0.965)	-1.2462	-0.6701	22.166	8.75E-09	C1 < C2, C1 < C3, C2 < C3
Lingual_R	-0.577 (0.837)	0.062 (0.797)	0.588 (0.895)	-1.3021	-0.5878	27.829	1.66E-10	C1 < C2, C1 < C3, C2 < C3
Occipital_Sup_L	-0.214 (0.477)	-0.134 (0.500)	0.518 (0.640)	-1.1437	-1.0194	31.469	1.39E-11	C1 < C3, C2 < C3
Occipital_Sup_R	-0.180 (0.719)	-0.082 (0.579)	0.377 (0.594)	-0.9387	-0.7727	11.969	1.87E-05	C1 < C3, C2 < C3
Occipital_Mid_L	-0.666 (1.158)	-0.062 (1.346)	0.934 (1.141)	-1.4024	-0.8734	23.167	4.20E-09	C1 < C2, C1 < C3, C2 < C3
Occipital_Mid_R	-0.494 (0.913)	-0.022 (0.770)	0.648 (0.819)	-1.3938	-0.8186	26.807	3.43E-10	C1 < C2, C1 < C3, C2 < C3
Occipital_Inf_L	-0.270 (0.574)	-0.097 (0.583)	0.517 (0.445)	-1.7683	-1.3804	31.237	1.55E-11	C1 < C2, C1 < C3, C2 < C3

	C1 (n=49)	C2 (n=76)	C3 (n=40)	C1 z-scores	C2 z-scores	F ANCOVA	FDR adjusted p-values	post-hoc paired test
Occipital_Inf_R	-0.338 (0.706)	-0.032 (0.670)	0.477 (0.629)	-1.2973	-0.8112	20.599	2.66E-08	C1 < C2, C1 < C3, C2 < C3
Fusiform_L	-0.631 (0.988)	0.027 (0.977)	0.721 (0.795)	-1.7004	-0.872	29.204	6.26E-11	C1 < C2, C1 < C3, C2 < C3
Fusiform_R	-0.726 (1.045)	0.160 (0.841)	0.584 (0.898)	-1.4588	-0.4713	30.798	2.06E-11	C1 < C2, C1 < C3, C2 < C3
Postcentral_L	-0.667 (1.061)	0.021 (1.003)	0.777 (1.319)	-1.0952	-0.5732	23.889	2.63E-09	C1 < C2, C1 < C3, C2 < C3
Postcentral_R	-0.553 (1.011)	0.061 (1.024)	0.560 (1.190)	-0.9353	-0.4187	15.241	1.34E-06	C1 < C2, C1 < C3, C2 < C3
Parietal_Sup_L	-0.482 (0.881)	0.090 (0.995)	0.419 (0.869)	-1.0374	-0.3782	13.364	5.86E-06	C1 < C2, C1 < C3
Parietal_Sup_R	-0.531 (0.819)	0.069 (0.774)	0.518 (0.857)	-1.2247	-0.5234	24.013	2.32E-09	C1 < C2, C1 < C3, C2 < C3
Parietal_Inf_L	-0.318 (0.450)	0.121 (0.423)	0.160 (0.468)	-1.0231	-0.0833	21.436	1.49E-08	C1 < C2, C1 < C3
Parietal_Inf_R	-0.370 (0.508)	0.064 (0.706)	0.332 (0.714)	-0.9839	-0.3746	16.386	5.71E-07	C1 < C2, C1 < C3, C2 < C3
SupraMarginal_L	-0.489 (0.746)	0.061 (0.752)	0.482 (0.669)	-1.4526	-0.6287	25.151	1.15E-09	C1 < C2, C1 < C3, C2 < C3
SupraMarginal_R	-0.391 (0.696)	0.023 (0.687)	0.433 (0.698)	-1.181	-0.5867	19.653	5.41E-08	C1 < C2, C1 < C3, C2 < C3
Angular_L	-0.329 (0.757)	0.075 (1.044)	0.261 (0.983)	-0.6011	-0.1894	5.587	0.0053932 58	C1 < C2, C1 < C3
Angular_R	-0.649 (0.963)	0.117 (1.209)	0.572 (1.101)	-1.1095	-0.4131	17.247	2.96E-07	C1 < C2, C1 < C3, C2 < C3
Precuneus_L	-0.938 (0.870)	0.054 (0.992)	1.045 (0.916)	-2.1652	-1.082	67.966	1.14E-20	C1 < C2, C1 < C3, C2 < C3
Precuneus_R	-0.902 (0.986)	0.041 (0.971)	1.026 (1.100)	-1.753	-0.8955	54.214	1.60E-17	C1 < C2, C1 < C3, C2 < C3
Paracentral_Lobule_L	-0.359 (1.050)	0.058 (0.854)	0.328 (0.972)	-0.7072	-0.277	7.396	0.0011162 79	C1 < C2, C1 < C3
Paracentral_Lobule_R	-0.305 (1.058)	0.012 (0.791)	0.351 (0.955)	-0.688	-0.3548	6.908	0.0011162 79	C1 < C3
Caudate_L	-0.0172 (0.335)	0.0001 (0.278)	0.021 (0.288)	-0.1331	-0.073	0.219	0.8124631 58	n.s
Caudate_R	-0.014 (0.387)	0.001 (0.324)	0.016 (0.317)	-0.0978	-0.05	0.109	0.897	n.s
Pallidum_L	-0.001 (0.049)	0.004 (0.059)	-0.007 (0.059)	0.1091	0.2079	0.668	0.5363478 26	n.s
Pallidum_R	-0.002 (0.040)	0.004 (0.055)	-0.005 (0.056)	0.0521	0.1751	0.562	0.5894193 55	n.s
Putamen_L	-0.036 (0.408)	0.001 (0.463)	0.042 (0.445)	-0.1788	-0.0941	0.428	0.6668936 17	n.s
Putamen_R	-0.094 (0.415)	0.019 (0.442)	0.080 (0.384)	-0.4546	-0.1588	2.436	0.096	n.s
Thalamus_L	-0.224 (0.288)	0.047 (0.247)	0.184 (0.322)	-1.2652	-0.4221	32.224	9.07E-21	C1 < C2, C1 < C3, C2 < C3
Thalamus_R	-0.182 (0.311)	0.028 (0.272)	0.169 (0.334)	-1.0503	-0.4191	19.548	5.74E-08	C1 < C2, C1 < C3, C2 < C3
Heschl_L	-0.158 (0.186)	0.028 (0.240)	0.138 (0.310)	-0.9548	-0.3528	21.207	1.74E-08	C1 < C2, C1 < C3, C2 < C3

	C1 (n=49)	C2 (n=76)	C3 (n=40)	C1 z-scores	C2 z-scores	F ANCOVA	FDR adjusted p-values	post-hoc paired test
Heschl_R	-0.090 (0.146)	0.013 (0.170)	0.084 (0.220)	-0.7907	-0.32	13.532	5.22E-06	C1 < C2, C1 < C3, C2 < C3
Temporal_Sup_L	-0.744 (1.003)	0.240 (1.150)	0.456 (1.219)	-0.9851	-0.1772	18.815	9.91E-08	C1 < C2, C1 < C3
Temporal_Sup_R	-0.666 (0.995)	0.171 (1.056)	0.490 (1.218)	-0.9497	-0.262	17.501	2.50E-07	C1 < C2, C1 < C3
Temporal_Pole_Sup_L	-0.216 (0.446)	0.048 (0.424)	0.174 (0.351)	-1.1124	-0.3588	12.995	7.92E-06	C1 < C2, C1 < C3
Temporal_Pole_Sup_R	-0.232 (0.405)	0.057 (0.375)	0.176 (0.430)	-0.9525	-0.2783	15.902	8.11E-07	C1 < C2, C1 < C3
Temporal_Mid_L	-0.759 (1.385)	-0.152 (1.295)	1.219 (1.356)	-1.4601	-1.0118	31.992	1.01E-11	C1 < C2, C1 < C3, C2 < C3
Temporal_Mid_R	-1.217 (1.566)	0.1202 (1.505)	1.262 (1.477)	-1.6794	-0.7736	38.769	1.23E-13	C1 < C2, C1 < C3, C2 < C3
Temporal_Pole_Mid_L	-0.217 (0.404)	0.017 (0.512)	0.234 (0.474)	-0.9531	-0.4579	12.478	1.22E-05	C1 < C2, C1 < C3, C2 < C3
Temporal_Pole_Mid_R	-0.338 (0.440)	0.048 (0.502)	0.322 (0.567)	-1.1643	-0.4826	24.79	1.37E-09	C1 < C2, C1 < C3, C2 < C3
Temporal_Inf_L	-0.842 (1.073)	0.077 (0.990)	0.885 (0.994)	-1.7377	-0.8131	42.058	1.76E-14	C1 < C2, C1 < C3, C2 < C3
Temporal_Inf_R	-1.166 (1.040)	0.132 (1.144)	1.177 (1.213)	-1.9321	-0.8613	65.704	2.63E-20	C1 < C2, C1 < C3, C2 < C3
Pons	-0.013 (0.030)	-0.001 (0.027)	0.018 (0.063)	-0.5069	-0.3069	8.84	0.0002697 76	C1 < C3, C2 < C3
Dorsal_Mesopontine	-0.002 (0.007)	-0.0003 (0.007)	0.003 (0.008)	-0.623	-0.4022	6.622	0.0021818 18	C1 < C3, C2 < C3
Entorhinal_Cortex_L	-0.074 (0.279)	0.016 (0.282)	0.059 (0.244)	-0.5489	-0.1779	3.474	0.0352	C1 < C3
Entorhinal_Cortex_R	-0.103 (0.195)	0.024 (0.262)	0.080 (0.2484)	-0.7415	-0.2234	8.599	0.0003312 48	C1 < C2, C1 < C3
ParaHippocampal_L	-0.092 (0.216)	0.003 (0.264)	0.1064 (0.218)	-0.9106	-0.4695	9.28	0.0001840 09	C1 < C2, C1 < C3, C2 < C3
ParaHippocampal_R	-0.135 (0.239)	0.022 (0.228)	0.122 (0.265)	-0.9707	-0.3781	16.249	6.29E-07	C1 < C2, C1 < C3, C2 < C3
Cingulum_Post_L	-0.078 (0.129)	0.004 (0.139)	0.087 (0.166)	-0.9985	-0.503	18.559	1.17E-07	C1 < C2, C1 < C3, C2 < C3
Cingulum_Post_R	-0.100 (0.166)	0.026 (0.154)	0.072 (0.169)	-1.0265	-0.2742	17.744	2.11E-07	C1 < C2, C1 < C3
Retrosplenial_Cortex_L	-0.119 (0.151)	0.010 (0.192)	0.126 (0.243)	-1.009	-0.4782	22.126	8.78E-09	C1 < C2, C1 < C3, C2 < C3
Retrosplenial_Cortex_R	-0.071 (0.126)	0.006 (0.135)	0.076 (0.150)	-0.9776	-0.4635	16.074	7.15E-07	C1 < C2, C1 < C3, C2 < C3

Mean (SD) of the residuals adjusted for center and ICV, calculated in the overall cohort. These values were used as the input data for the data-driven random forest-based cluster analysis. Additionally, for plotting purposes in figure 1, the z-score values were calculated for C1 and C2 groups from the residuals adjusted for age, using C3 as the reference group.

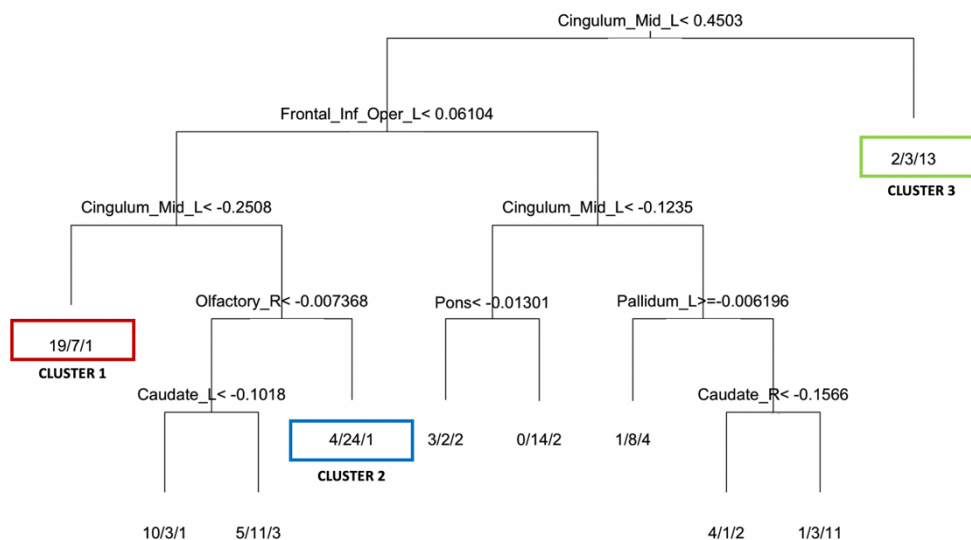
Abbreviations: C1 – Cortical predominant subtype; C2 – Fronto-occipital predominant subtype; C3 – Cortical predominant subtype; ICV – intracranial volume; SD – standard deviation.

Supplementary Table 3. ROIs with the highest contribution to the cluster analysis.

10 TOP ROIs	Gini Index
Right Pallidum	0.9521002
Left frontal inferior operculum	0.9675189
Left Olfactory cortex	0.9774211
Left Pallidum	0.9898548
Left middle cingulum	0.9928215
Pons	0.9928266
Left Caudate	0.9935472
Right Caudate	0.9976649
Right Olfactory cortex	1.0100825
Left Putamen	1.0108899

The 10 ROIs with the lowest Gini Index values. The mean decrease in the Gini index was used to identify the ROIs with the highest contribution to the cluster analysis.

Supplementary Figure 3. Supervised classification tree.



Supervised classification tree showing the complete view of the variable discrimination rules for the DLB clusters. Among the 10 most relevant ROIs, the left middle cingulum, which showed greater volumes in C3 compared to C1 and C2, was placed on top of the tree, indicating that it was the most relevant ROI to discriminate between the DLB clusters. Then, the tree was divided into 2 branches: one that included C1 and C2, and another one for C3. The branch including C1 and C2 had the left opercular inferior frontal on top of the branch, which had a greater GM volume in C3 compared to C1 and C2, but it did not differ between C1 and C2. Next, the right olfactory cortex was able to discriminate between C1 and C2, with C2 showing larger GM volumes than C1.

Supplementary Table 4. Longitudinal analysis of MMSE trajectories.

timepoint = MMSE baseline							
contrast	estimate	SE	df	t-stat	p-value	Lower CL	Upper CL
1-2	-1.31	0.987	188	-1.33	0.3806	-3.64	1.0196
1-3	-2.79	1.145	188	-2.433	0.0419	-5.49	-0.0805
2-3	-1.47	1.052	188	-1.4	0.3428	-3.96	1.0122
timepoint = MMSE 12months							
contrast	estimate	SE	df	t-stat	p-value	Lower CL	Upper CL
1-2	-1.95	1.103	260	-1.766	0.1831	-4.55	0.6523
1-3	-4.59	1.234	236	-3.719	0.0007	-7.5	-1.6787
2-3	-2.64	1.148	244	-2.3	0.0577	-5.35	0.0672
timepoint = MMSE 24months							
contrast	estimate	SE	df	t-stat	p-value	Lower CL	Upper CL
1-2	-2.35	1.173	297	-2.006	0.1124	-5.11	0.4094
1-3	-4.96	1.288	265	-3.847	0.0004	-7.99	-1.9204
2-3	-2.6	1.193	270	-2.182	0.076	-5.42	0.208
timepoint = MMSE 36months							
contrast	estimate	SE	df	t-stat	p-value	Lower CL	Upper CL
1-2	-2.14	1.551	350	-1.382	0.3517	-5.8	1.5083
1-3	-6.57	1.643	355	-4	0.0002	-10.44	-2.7039
2-3	-4.43	1.46	352	-3.032	0.0073	-7.86	-0.9902

The method used for degrees of freedom was the Kenward-Roger method, and the p-value adjustment was carried out with the Tukey method for comparing a family of 3 estimates. A confidence level (CL) of 0.95 was used.